Congenital Malformations Registry
Monitoring for Changes in Birth Defects Prevalence

NBDPN 10th Annual Meeting
San Antonio, Texas
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Congenital Malformations Registry

Background

• Established October, 1982

• Recognition of the environment as a potential etiologic factor for birth defects (Love Canal)

• Reporting to the Registry is mandated by Public Health Law - State Sanitary Code 22.3
Congenital Malformations Registry

Background

Population Coverage: Statewide approximately 260,000 to 300,000 births annually

Designed for surveillance, research & to provide data to health programs to aid in the development of needs assessment

Full time staff - 7.5
Grant funded positions - 12
Registry receives approximately 15,000 electronic reports per year from 165 hospitals statewide on 10,000-11,000 children diagnosed up to the age of 2.

Cases can be diagnosed with 20+ major malformations.

Cases can be reported multiple times from one or more hospitals & by physicians.

Reports from all sources are maintained and linked with a unique case number.
Data Linkage

CMR reports are matched with Vital Records & SPARCS hospital discharge files to check the completeness and accuracy of the data and to collect additional variables.

CMR data
(Unique records of children reported to CMR)

- Birth Certificate
- Death Certificate
- SPARCS

Audits
CMR Birth Defects Surveillance
Previous System

- Performed in January and July

- Analysis by Health Service Areas (HSA), with HSA 3 & 4 combined due to small number of births

- Compare prevalence of surveillance malformations among infants born in the January to June or July to December time period to same time period for the baseline years
Why change to monitoring for variations in space and changes in time & space?

- Mapping and spatial analysis software are readily available and becoming more user friendly

- Increasing availability of geo-referenced environmental and sociodemographic data - State Health Departments

- Can be used as a tool to assess completeness of reporting and detect potential deficiencies

- Additional way to monitor birth defects reporting statewide and to target hospitals for site visits and audits
Why change to monitoring for variations in space and changes in time & space?

- Having procedures in place allows for an informed and quick response to community concerns about possible clusters and environmental exposures.

- Small area spatial analysis allows for the investigation of identified geographically localized potential hazards.

- Provide guidance for public health interventions.

- Ultimate goal of being able to detect significant clusters from a statistical and public health point of view.
detecting clustering of birth defects remains a challenge when health events are rare, poorly diagnosed or not adequately reported

need to avoid generating a multitude of statistically significant results with limited ability to follow-up

caution should be taken in interpreting maps & results of spatial analysis as errors in registry or vital statistics data could result in erroneous conclusions

* Webster’s New Collegiate Dictionary
Congenital Malformations Registry

Background

- Established October, 1982
- Recognition of the environment as a potential etiologic factor for birth defects (Love Canal)
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Caveats

- geographic bias/errors can be introduced through the use of automated geocoding software (Gregorio et al. 1999)

- costly and time consuming to accurately geocode large health outcome data sets particularly in rural areas where exact street address information is unavailable

- data collection must ensure that the data are complete and valid

- identification of cause or knowledge about etiology is unlikely to arise from the study of most clusters (Sever, 1994)

- recommend involving experts from various backgrounds to work together to avoid the caveats of GIS (Kirby, 1996)
CMR Surveillance Tests for Clustering

Time
- Clusters:
  - Grimson
  - Larson
  - Empty Cell
- When:
  - Scan
  - Cusum
- Seasonal:
  - Edward's
  - Hewitt
  - Tango
- Moran's I
- Geary C
- Joint Count
- Nearest Neighbor

Space
- Are the cases clustered? (Global)
- Location of most likely cluster? (Local)
- Are cases clustered in Time & Space? (Global)
- Where & when did most likely cluster occur? (Local)

Time & Space
- Knox
- Jacquez k
- Nearest Neighbor
- Grimson's
- Spatial Scan (Space-Time Permutation)

Spatially Weighted Regression Analysis

Focal Tests for Clustering
Availability

- SatScan (Spatial Scan; Space-Time Permutation)
- DMap (Spatial filtering)
- CrimeStat (Local Moran’s I; Contouring)
- GeoDa (Local Moran’s I; Spatially weighted regression)
- Cluster Seer -$$ (24 space time tests)
  - Boundary Seer
  - SpaceStat
- CDC / MACDP developing Automated Spatial Surveillance Project (ASSP)
Possible Defects to Monitor

<table>
<thead>
<tr>
<th>Rank</th>
<th>Malformations</th>
<th>Malformations</th>
</tr>
</thead>
<tbody>
<tr>
<td>High</td>
<td>01) Anencephalus(BPA=740.0)</td>
<td>01) Anencephalus(BPA=740.0)</td>
</tr>
<tr>
<td>High</td>
<td>02) Spina Bifida W/o Anencephalus(BPA=741.0)</td>
<td>02) Spina Bifida W/o Anencephalus(BPA=741.0)</td>
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<tr>
<td>High</td>
<td>03) Encephalocele(BPA=742.0)</td>
<td>03) Encephalocele(BPA=742.0)</td>
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<tr>
<td>High</td>
<td>04) Aniridia(BPA=743.42)</td>
<td>04) Aniridia(BPA=743.42)</td>
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<tr>
<td>High</td>
<td>05) Common Truncus(BPA=745.0)</td>
<td>05) Common Truncus(BPA=745.0)</td>
</tr>
<tr>
<td>High</td>
<td>06) Transposition of Great Arteries(BPA=745.01)</td>
<td>06) Transposition of Great Arteries(BPA=745.01)</td>
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<tr>
<td>High</td>
<td>07) Tetralogy of Fallot(BPA=745.2 &amp; 746.84)</td>
<td>07) Tetralogy of Fallot(BPA=745.2 &amp; 746.84)</td>
</tr>
<tr>
<td>High</td>
<td>08) Hypoplastic Left Heart Syndrome(BPA=740.70)</td>
<td>08) Hypoplastic Left Heart Syndrome(BPA=740.70)</td>
</tr>
<tr>
<td>High</td>
<td>09) Single/Common ventricle(BPA=745.300)</td>
<td>09) Single/Common ventricle(BPA=745.300)</td>
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<tr>
<td>High</td>
<td>10) Cleft Palate w/o Cleft Lip(BPA=749.0)</td>
<td>10) Cleft Palate w/o Cleft Lip(BPA=749.0)</td>
</tr>
<tr>
<td>High</td>
<td>11) Cleft Lip w/ w/o Cleft Lip(BPA=749.1 &amp; 749.2)</td>
<td>11) Cleft Lip w/ w/o Cleft Lip(BPA=749.1 &amp; 749.2)</td>
</tr>
<tr>
<td>High</td>
<td>12) Choanal Atresia(BPA=748.0)</td>
<td>12) Choanal Atresia(BPA=748.0)</td>
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<tr>
<td>High</td>
<td>13) Esophageal Atresia/Tracheoesophageal Fistula(BPA=750.3)</td>
<td>13) Esophageal Atresia/Tracheoesophageal Fistula(BPA=750.3)</td>
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<tr>
<td>High</td>
<td>14) Pyloric Stenosis(BPA=750.54)</td>
<td>14) Pyloric Stenosis(BPA=750.54)</td>
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<tr>
<td>High</td>
<td>15) Renal Agenesis/Hypoplasia(BPA=753.0)</td>
<td>15) Renal Agenesis/Hypoplasia(BPA=753.0)</td>
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<tr>
<td>High</td>
<td>16) Bladder Exstrophy(BPA=753.50)</td>
<td>16) Bladder Exstrophy(BPA=753.50)</td>
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<tr>
<td>High</td>
<td>17) Cloacal Exstrophy/persistent cloaca(BPA=754.550)</td>
<td>17) Cloacal Exstrophy/persistent cloaca(BPA=754.550)</td>
</tr>
<tr>
<td>High</td>
<td>18) Hypospadias &amp; Epispadias(BPA=752.3)</td>
<td>18) Hypospadias &amp; Epispadias(BPA=752.3)</td>
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<tr>
<td>High</td>
<td>19) Diaphragmatic Hernia(BPA=756.61)</td>
<td>19) Diaphragmatic Hernia(BPA=756.61)</td>
</tr>
<tr>
<td>High</td>
<td>20) Trisomy 13(BPA=758.1)</td>
<td>20) Trisomy 13(BPA=758.1)</td>
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<tr>
<td>High</td>
<td>21) Down Syndrome(BPA=758.0)</td>
<td>21) Down Syndrome(BPA=758.0)</td>
</tr>
<tr>
<td>High</td>
<td>22) Trisomy 18(BPA=758.2)</td>
<td>22) Trisomy 18(BPA=758.2)</td>
</tr>
<tr>
<td>Medium/High</td>
<td>23) Anotia/Microtia(BPA=744.01 &amp; 744.21)</td>
<td>23) Anotia/Microtia(BPA=744.01 &amp; 744.21)</td>
</tr>
<tr>
<td>Medium/High</td>
<td>24) Endocardial Cushion Defect(BPA=745.6)</td>
<td>24) Endocardial Cushion Defect(BPA=745.6)</td>
</tr>
<tr>
<td>Medium/High</td>
<td>25) Ebstein's Anomaly(BPA=746.20)</td>
<td>25) Ebstein's Anomaly(BPA=746.20)</td>
</tr>
<tr>
<td>Medium/High</td>
<td>26) Rectal &amp; Large Intestinal Atresia/Stenosis(BPA=751.2)</td>
<td>26) Rectal &amp; Large Intestinal Atresia/Stenosis(BPA=751.2)</td>
</tr>
<tr>
<td>Medium/High</td>
<td>27) Reduction Deformity, Upper Limbs(BPA=755.2)</td>
<td>27) Reduction Deformity, Upper Limbs(BPA=755.2)</td>
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<tr>
<td>Medium/High</td>
<td>28) Reduction Deformity, Lower Limbs(BPA=755.3)</td>
<td>28) Reduction Deformity, Lower Limbs(BPA=755.3)</td>
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<tr>
<td>Medium/High</td>
<td>29) Sacral agenesis(BPA=756.170)</td>
<td>29) Sacral agenesis(BPA=756.170)</td>
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<tr>
<td>Medium</td>
<td>30) Hydrocephalus w/o Spina Bifida(BPA=742.3)</td>
<td>30) Hydrocephalus w/o Spina Bifida(BPA=742.3)</td>
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<tr>
<td>Medium</td>
<td>31) Microcephalus(BPA=742.10)</td>
<td>31) Microcephalus(BPA=742.10)</td>
</tr>
<tr>
<td>Medium</td>
<td>32) Anophthalmia/Microophthalmia(BPA=743.00-743.10)</td>
<td>32) Anophthalmia/Microophthalmia(BPA=743.00-743.10)</td>
</tr>
<tr>
<td>Medium</td>
<td>33) Congenital Cataract(BPA=743.32)</td>
<td>33) Congenital Cataract(BPA=743.32)</td>
</tr>
<tr>
<td>Medium</td>
<td>34) Atrial Septal Defect(BPA=745.51-745.59)</td>
<td>34) Atrial Septal Defect(BPA=745.51-745.59)</td>
</tr>
<tr>
<td>Medium</td>
<td>35) Tricuspid Valve Atresia &amp; Stenosis(BPA=746.10)</td>
<td>35) Tricuspid Valve Atresia &amp; Stenosis(BPA=746.10)</td>
</tr>
<tr>
<td>Medium</td>
<td>36) Aortic Valve Stenosis(BPA=746.30)</td>
<td>36) Aortic Valve Stenosis(BPA=746.30)</td>
</tr>
<tr>
<td>Medium</td>
<td>37) Coarctation of Aorta(BPA=747.1)</td>
<td>37) Coarctation of Aorta(BPA=747.1)</td>
</tr>
</tbody>
</table>
Defects to Monitor – Additional Considerations

- monitor for the occurrence of various grouped defects (pathogenetically similar) defects to increase power e.g. NTDs

- monitor for multiple malformations excluding specific sequences

- monitor for selected multiple malformation combinations

- monitor occurrence of surveillance defects as isolated or in combination with other defects (e.g. cleft lip vs. cleft lip with Trisomy 13)

- groups to monitor based on embryology?
Spatial Scan Statistic

- Circular search “window’ is positioned on centroid of each ZIP code and expanded to a pre-defined limit (%5 of all births)

- For each window, the likelihood ratio of finding the observed number of cases, relative to number of births, inside and outside the circle is compared.

- Statistical significance determined through Monte Carlo testing
Most Likely Clusters of Low Birthweight Births Using Spatial Scan Statistic

p<0.05 Restictions; no cluster can contain more than 10% of births.
Congenital malformations clusters identified using the scan statistic at p<.05 in NYS, 1992-1995
Spatial Filters

• Population based spatial smoothing method

• Can be used on individual and group level data

• Simultaneously computes rates and p-values using MLR and Monte Carlo simulations to identify significantly elevated areas.

• Used at multiple resolutions (population size)
Spatial Filtering
Local Cluster Tests

• Turnbull’s method
• Besag and Newell’s method

• Both use group level data (#cases/births)
• A circular window is centered on each region and expand outward until:
  – Minimum population size met (Turnbull)
  – Minimum number of cases met (Besag-Newell)
• Compare rate inside vs. outside circle
• Use Monte Carlo simulations to test for significance
Significant Clusters of Down's Syndrome Identified by SatScan

No overlapping clusters; maximum of 5% of births captured by a cluster
Purely Spatial analysis
scanning for clusters with
high or low rates using the Poisson model.

SUMMARY OF DATA

Number of ZIP Codes: 548
Total population ......: 442,935
Total cases ...........: 456
Annual cases / 10,000.: 10.3

MOST LIKELY CLUSTER

ZIP Codes included.: 14001
Coordinates / radius.: (43.0438 N, 78.4965 W) / 0.00 km
Births..............: 835
Number of cases....: 5 (0.86 expected)
Overall relative risk.: 5.8
Log likelihood ratio.: 4.7
Monte Carlo rank....: 9,685/10,000
P-value...............: 0.9685
Recommendations

• Evaluate the results of several clustering programs and compare and contrast the results

• Check data quality by region to assure consistency across the state

• To investigate clusters around a putative source of pollution use a focused test.

• Cluster detection methods are most suitable for exploratory data analysis (hypothesis generating)
  – Once hypotheses have been generated they need to be tested with more formal epidemiological studies
Recommendations

• Many time-space clusters will be due to chance and care must be taken in selecting which alarms to follow-up

• Consideration given to not only to statistical significance but to the absolute number of events

• To investigate a “significant” cluster recommend following methodology similar to that outlined by the CBDMP (Harris et al., 1999) also a NCBDDDD paper in Teratology by (Williams et al., 2002)

• Recommend article by Siffel et al. 2006 in Birth Defects Research Part A-describes role of GIS in birth defects surveillance & research
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